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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,113	12/04/2003	Guy Bemis	VPI/01-116 DIV US	7647

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/728,113	BEMIS ET AL.	
	Examiner	Art Unit	
	Deepak Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,26-29 and 31-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-5, 26-29 and 31-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This office action is in response to the amendment filed on June 15, 2006.

Claims 1, 3-5, 26-29 and 31-34 are pending in this application.

Withdrawn Rejections/Objections:

Applicant is notified that any outstanding rejection/objection that is not expressly maintained in this office action has been withdrawn or rendered moot in view of applicant's amendments and/or remarks.

The following rejections are maintained:

1. Claims 28, 29, 31 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment of rheumatoid arthritis, does not reasonably provide enablement for the treatment of all other Src- or Lck-mediated diseases embraced by the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The reasons provided in the previous office action are incorporated here by reference.

Applicant's arguments have been fully considered but they were not deemed to be persuasive. Applicant argues that 'claim 28 recites a method of inhibiting Src or Lck activity in a biological sample *in vitro* and specification pages 69-74 describe the *in vitro* activity of the compounds'. Applicant's arguments have been fully considered but they were not deemed to be persuasive. The instant claim is drawn to 'a method of inhibiting Src- or Lck-activity in a

·biological sample *in vitro*' and the term "biological sample" is defined in the specification (page 58, lines 17-21) to 'include, without limitation, cell cultures or extracts thereof; biopsied material obtained from a mammal or extracts thereof; and blood, saliva, urine, feces, semen, tears, or other body fluids or extracts thereof'. As can be seen from the definition of the term "biological sample" and the purpose of the inhibition of or Src- or Lck-activity which includes for example, blood transfusion, organ-transplantation, etc. As the inhibition of Src- or Lck-activity in a biological sample is disclosed to be useful for blood transfusion, organ-transplantation, etc., it implicitly reads on the inherent therapeutic methods characterized by the activity, which as per the specification includes numerous types of disorders.

The testing assays provided in the specification at page 70 is to test the ability of the compounds to inhibit Src activity using a standard coupled enzyme system, however, there is insufficient guidance in the disclosure regarding the provided assay. First, the specification provides that the coupled enzyme system is provided in Fox et al., however, the cited article deals with inhibition of p38 MAP kinase activity. Next, applicant has not provided how this correlates with the efficacy in all types of biological samples encompassed by the instant method and their use in the various purposes wherein the inhibition activity is useful. For example, blood transfusion is the process of transferring blood or blood-based products from one person into the circulatory system of another. Blood transfusions may be seen as a procedure to treat some medical conditions, such as massive blood loss due to trauma, surgery, shock and where the red cell producing mechanism (or some other normal and essential component) fails. Similarly, an organ transplantation is the transplantation of a whole or partial organ from one body to another (or from a donor site on the patient's own body), for the purpose of replacing the

recipient's damaged or failing organ with a working one from the donor site. As can be seen from the above, without limitation these purposes are intended for therapeutic methods and applicant has not provided competent evidence sufficient to enable the claimed method.

Further, the instantly claimed method alternatively recites the use of 'a composition according to claim 26', which composition comprises 'the compound of formula I and a pharmaceutically acceptable carrier, adjuvant or vehicle' as being added to the biological sample. A pharmaceutical composition of the kind recited in the instant claims is generally used for internal adminstration type therapeutic methods. Therefore, the instant claim appears to be directed to the various types of therapeutic methods associated with Src- or Lck-inhibition activity. Therefore, it is maintained that applicants have not provided sufficient test assays or data to support the method of inhibition commensurate in scope with the claim.

With regards to claims 29, 31 and 32, applicant argues that 'the claims have been amended to recite methods of treating specific diseases or disorders and the nexus between Src or Lck inhibition and the treatment of diseases was well established at the time of the invention'. However, some of the cited references were not state of the art as of the filing of the application, see e.g., Goldberg (2003), Myoui (2003). Evidence that the compounds are effective in the treatment of claimed disorders must have been available as of the filing date in order to provide an enabling disclosure. For example, all the references cited to demonstrate the claimed compounds to be effective in the treatment of T-cell mediated diseases, bone metastasis, etc. were all published after the effective filing date of the instant application.

Applicant relies on the references cited as Exhibits A-K (including Rahim et al., Weiner et al., and Staley et al., to provide the link between Src or Lck and the claimed methods of

treatment including treatment of lupus, cancer selected from colon cancer, breast cancer, hepatic cancer, pancreatic cancer, B-cell leukemia or lymphoma, an autoimmune disease, an allergy, etc. As submitted by applicant, each of the reference appears to provide link between Src and a specific disorder, i.e., for example, Weiner and Staley (colon tumor). The references do not appear to provide enablement for the scope of the instant claim reciting a method of treatment of the assorted diseases of the instant claims. The state of the art does not provide how the data disclosed in the specification can be extrapolated to the treatment of all types of diseases related to the Src biochemical pathways recited in the instant claims, and the diseases having diverse etiologies - hypercalcemia, osteoporosis, osteoarthritis, various cancers, bone metastasis, paget's disease, etc. While the specification provides sufficient enabling disclosure for the synthesis of the instantly claimed compounds, does not provide an enabling disclosure sufficient to cover the entire scope of the methods of use recited in the instant claims.

Applicant has not provided sufficient evidence that establishes that the disclosure would have enabled for one skilled in the art at the time of filing. Further, the state of the art does not identify a single class of compounds that can treat all types of diseases of the instant claims. Further, one skilled in the art of medicinal therapy recognizes that there are complex interactions between individual genetic, developmental state, sex, dietary, environmental, drug, and lifestyle factors that contribute to the carcinogenic process, making it even more challenging to have a single therapeutic agent for the treatment of diverse diseases. Rigorously planned and executed clinical trials, incorporating measurement of appropriate biomarkers and pharmacodynamic endpoints are critical for selecting the optimal dose and schedule. A detailed understanding of the molecular mode of action of the Lck and Src kinases, alongside the elucidation of the

molecular pathology of individual diseases is required to identify disease types and individual patients that may benefit most from treatment. It is also important to construct a pharmacologic audit trail linking molecular biomarkers and pharmacokinetic and pharmacodynamic parameters to receptor response endpoints. Therefore, it is maintained that applicants have not provided sufficient test assays or data to support the method of inhibition or treatment commensurate in scope with the claims, as of the filing date of the application.

2. Claims 1 and 3-5 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,689,778, for the reasons provided in the previous office action which are incorporated here by reference. It is acknowledged that 'applicants will provide a terminal disclaimer over the '778 patent upon indication of allowable subject matter'.

The following rejections are necessitated by the amendment:

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29 and 32-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. Claims 29 and 32 contains the trademark/trade name, see for example: Gleevec™, Aricept®, etc. Where a trademark or trade name is used in a claim as a limitation to

identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an additional therapeutic agent and, accordingly, the identification/description is indefinite.

2. Claim 33 recites the limitation "said implantable device" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 3-5, 26-29 and 31-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Green et al., WO 01/12621. The reference teaches pyrimidine compounds having kinase inhibitory activity, see formula (I) in page 8 and the compounds of the Examples in Tables 1-7. The reference compounds are unsubstituted at the 5-position of the pyrimidine as compared to the instantly claimed compounds which recite a substituent R^1. According to the instant claims definition of R^1 includes T_yR wherein y is 1; T is an alkylidene group (e.g., $-CH_2-$) and R can be H and therefore, R^1 of the instant claims includes a methyl group. Therefore, the instantly

claimed compounds differ from the reference compounds by a -CH_2 group and it is well established that compounds that differ by a –CH_2 group are structural homologs. It would have been obvious to one having ordinary skill in the art at the time of the invention to modify the reference compounds to prepare the structural homolog. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally homologous compounds are expected to possess similar properties. It has been held that compounds that are structurally homologous to prior art compounds are *prima facie* obvious, absent a showing of unexpected results. *In re Hass*, 60 USPQ 544 (CCPA 1944); *In re Henze*, 85 USPQ 261 (CCPA 1950).

Note: Applicant argues that Green (WO 01/12621 A2 published February 22, 2001) is not a proper reference under 35 U.S.C. 102(b) as the instant application claims priority to U.S. Provisional Application 60/302,969, filed July 3, 2001. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims of instant application. See the differences between the provisional application and the instant application in the definitions of some of the variables:

Variable	60/302,969	10/728,113
T	T is an optionally substituted, straight or branched C_1-C_6 aliphatic group wherein a non-terminal methylene unit of T is optionally replaced by O, NR, NRC(O), C(O)NR, C(O), S, SO, or SO_2	T is independently selected from an optionally substituted C_1-C_6 alkylidene chain, wherein: a methylene unit of T is optionally replaced by O, NR, NRC(O), C(O)NR, **NRC(O)NR**, C(O), **C(O)CH2C(O), C(O)C(O), C(O)O, OC(O), $NRSO_2$**, S, SO, **SO_2NR** or SO_2
X	X is selected from O, S, SO, SO_2, NH, C(O), C(O)NH, NHC(O), SO_2NH, or $NHSO_2$	X is selected from O, S, SO, SO_2, NH, C(O), C(O)NH, NHC(O), **NHC(O)NH**, SO_2NH, $NHSO_2$ or **$NHSO_2NH$**

Ar^1	Ar^1 is an optionally substituted five or six membered ring selected from aryl, heteroaryl, carbocyclyl or heterocyclyl	Ar^1 is independently selected from an optionally substituted ring selected from a 5-7 membered saturated, partially unsaturated, or fully unsaturated monocyclic ring having 0-3 heteroatoms

(The above table provides comparison of a representative list of variables of the instant claims). As the Provisional application does not fully support the instant claims, the effective filing date for the instant claims is the filing date of the parent application 10/171,895 filed June 14, 2002.

Double Patenting

Claims 1, 3-5, 26-29 and 31-33 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,693,108. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims substantially overlap the reference claims. See the reasons provided in the rejection under 35 U.S.C. 103.

Applicant argues that 'the amended claims recite compounds of formula I, wherein R^1 is not a hydrogen whereas analogous claims of the '108 patent recite compounds in which the substituent corresponding to R^1 is hydrogen'. However, as indicated in the 103 rejection above, the instantly claimed compounds are structural homologs of the reference compounds are therefore, would have been obvious to one of ordinary skill in the art.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

August 17, 2006